

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
31 March 2005 (31.03.2005)

PCT

(10) International Publication Number
WO 2005/028676 A2

(51) International Patent Classification⁷: **C12Q 1/68**,
C12N 9/10

KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number:
PCT/JP2004/014438

(22) International Filing Date:
24 September 2004 (24.09.2004)

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/505,571 24 September 2003 (24.09.2003) US

Declarations under Rule 4.17:

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

(71) Applicants (for all designated States except US): **ONCOTHERAPY SCIENCE, INC.** [JP/JP]; 3-16-13, Shirokanedai, Minato-ku, Tokyo 1080071 (JP). **THE UNIVERSITY OF TOKYO** [JP/JP]; 3-1, Hongo 7-chome, Bunkyo-ku, Tokyo 1138654 (JP).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **NAKAMURA, Yusuke** [JP/JP]; 17-33, Azamino 1-chome, Aoba-ku, Yokohama-shi, Kanagawa 2250011 (JP). **KATAGIRI, Toyomasa** [JP/JP]; 5-4-14-402, Higashigotanda, Shinagawa-ku, Tokyo 1410022 (JP). **NAKATSURU, Shuichi** [JP/JP]; 6-2, Shimoochiai 2-chome, Chuo-ku, Saitama-shi, Saitama 3380002 (JP).

(74) Agents: **SHIMIZU, Hatsushi** et al.; Kantetsu Tsukuba Bldg. 6F, 1-1-1, Oroshi-machi, Tsuchiura-shi, Ibaraki 3000847 (JP).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,

Published:

- without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD OF DIAGNOSING BREAST CANCER

(57) Abstract: Objective methods for detecting and diagnosing breast cancer (BRC) are described herein. In one embodiment, the diagnostic method involves determining the expression level of a BRC-associated gene that discriminates between BRC cells and normal cells. In another embodiment, the diagnostic method involves determining the expression level of a BRC-associated gene that discriminates among BRC cells, between DCIS and IDC cells. The present invention further provides means for predicting and preventing breast cancer metastasis using BRC-associated genes having unique altered expression patterns in breast cancer cells with lymph-node metastasis. Finally, the present invention provides methods of screening for therapeutic agents useful in the treatment of breast cancer, methods of treating breast cancer and method for vaccinating a subject against breast cancer.

WO 2005/028676 A2

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
31 March 2005 (31.03.2005)

PCT

(10) International Publication Number
WO 2005/028676 A3

(51) International Patent Classification⁷: C12Q 1/68,
C12N 9/10

TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(21) International Application Number:
PCT/JP2004/014438

(22) International Filing Date:
24 September 2004 (24.09.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/505,571 24 September 2003 (24.09.2003) US

(71) Applicants (for all designated States except US):
ONCOTHERAPY SCIENCE, INC. [JP/JP]; 3-16-13,
Shirokanedai, Minato-ku, Tokyo 1080071 (JP). **THE UNI-
VERSITY OF TOKYO** [JP/JP]; 3-1, Hongo 7-chome,
Bunkyo-ku, Tokyo 1138654 (JP).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **NAKAMURA,**
Yusuke [JP/JP]; 17-33, Azamino 1-chome, Aoba-ku,
Yokohama-shi, Kanagawa 2250011 (JP). **KATAGIRI,**
Toyomasa [JP/JP]; 5-4-14-402, Higashigotanda, Shina-
gawa-ku, Tokyo 1410022 (JP). **NAKATSURU, Shuichi**
[JP/JP]; 6-2, Shimoochiai 2-chome, Chuo-ku, Saitama-shi,
Saitama 3380002 (JP).

(74) Agents: **SHIMIZU, Hatsushi** et al.; Kantetsu Tsukuba
Bldg. 6F, 1-1-1, Oroshi-machi, Tsuchiura-shi, Ibaraki
3000847 (JP).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii)) for the following design-
ations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW,
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ,
EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM,
ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA,
SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG)

— as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii)) for all designations

Published:

— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
15 September 2005

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: METHOD OF DIAGNOSING BREAST CANCER

(57) Abstract: Objective methods for detecting and diagnosing breast cancer (BRC) are described herein. In one embodiment, the diagnostic method involves determining the expression level of a BRC-associated gene that discriminates between BRC cells and normal cells. In another embodiment, the diagnostic method involves determining the expression level of a BRC-associated gene that discriminates among BRC cells, between DCIS and IDC cells. The present invention further provides means for predicting and preventing breast cancer metastasis using BRC-associated genes having unique altered expression patterns in breast cancer cells with lymph-node metastasis. Finally, the present invention provides methods of screening for therapeutic agents useful in the treatment of breast cancer, methods of treating breast cancer and method for vaccinating a subject against breast cancer.

WO 2005/028676 A3